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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,617	05/14/2001	Jerome B. Zeldis	9516-022	7262

20582 7590 11/28/2007

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EXAMINER	
LEWIS, PATRICK T	
ART UNIT	**PAPER NUMBER**
1623	

MAIL DATE	DELIVERY MODE
11/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/853,617	ZELDIS ET AL.	
	Examiner	Art Unit	
	Patrick T. Lewis	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-11,61 and 62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 8-11 and 61-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I in the reply filed on February 28, 2003 is acknowledged. The requirement was made FINAL in the Office Action dated May 19, 2003.

Applicant's Response Dated March 8, 2007

2. Claims 1-4, 8-11 and 61-62 are pending. An action on the merits of claims 1-4, 8-11 and 61-62 is contained herein below.

3. The rejection of claims 1-4, 8-11 and 61-62 under 35 U.S.C. 103(a) as being unpatentable over Marx et al. Proc. Am. Soc. Clin. Onocology (1997), Vol. 18, No. 1751, page 454a (Marx) and Houghton et al. Cancer Chemother Pharmacol (1995), Vol. 36, pages 393-403 (Houghton) in combination is maintained for the reasons of record as set forth in the Office action dated June 14, 2007.

Rejections of Record as set forth in the Office Action dated June 14, 2007

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 1-4, 8-11 and 61-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marx et al. Proc. Am. Soc. Clin. Onocology (1997), Vol. 18, No. 1751,

page 454a (Marx) and Houghton et al. Cancer Chemother Pharmacol (1995), Vol. 36, pages 393-403 (Houghton) in combination.

Claims 1-4, 8-11 and 61-62 are drawn to a method of treating primary or metastatic cancer comprising administering a therapeutically elective amount of topotecan, or a pharmaceutically acceptable prodrug, salt, solvate, hydrate, or clathrate thereof, and a therapeutically effective amount of thalidomide, or a pharmaceutically acceptable salt or solvate thereof.

Marx teaches thalidomide as an antiangiogenic agent in the treatment of advanced cancer (1751). The cancers that are treated include brain, melanoma, breast, colon, mesothelioma and renal cell carcinoma. Thalidomide was administered as an oral daily dose of 100 to 500 mg/day.

Marx differs from the instantly claimed invention in that Marx does not teach the co-administration of topotecan. However, the deficiencies of Marx would have been obvious to one of ordinary skill in the art at the time of the invention when viewed in combination with the teachings Houghton.

Houghton teaches the efficacy of protracted schedules of therapy of topotecan and irinotecan against a panel of 21 human tumor xenografts derived from adult and pediatric malignancies (Abstract). Tumors included eight colon adenocarcinomas. Topotecan was administered by oral gavage 5 days per week for 12 consecutive weeks.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine thalidomide and topotecan for the treatment of colon cancer. As supported by *Ex parte Quadrantil*, 25 USPQ2d 1071 (Bd. Pat. Appl. & Inter. 1992), the

use of materials in combination, each of which is known to function for intended purpose, is *prima facie* obvious. In the absence of some proof of a secondary nature or of some specific limitations which would tip the scale of patentability in the favor of the instantly claimed invention, it would have been obvious to one of ordinary skill in this art at the time of the invention to co-administer two components (thalidomide and topotecan), each of which is recognized as having anti-cancer activity as applicant has done with the above cited references before them. Topotecan and thalidomide are well recognized in the art for the treatment of cancer individually, and to combine these two compounds or prodrugs, salts or solvates thereof to obtain the same result is indeed *prima facie* obvious.

6. Applicant's arguments filed September 10, 2007 have been fully considered but they are not persuasive. Applicant argues that 1) it would not have been obvious to combine the teachings of Marx and Houghton and 2) sufficient unexpected results have been provided to rebut any presumption of obviousness.

Applicant's arguments have been noted; however, as set forth supra, both topotecan and thalidomide were well recognized in the art for the treatment of cancer individually at the time of the instant invention. The only difference is the combination of the "old elements" (topotecan and thalidomide) into a single treatment regimen; however, Houghton explicitly teaches the treatment of cancer using a topoisomerase I inhibitor (topotecan) in combination with other cytotoxic agents (page 394, column 1). The skilled artisan would have been motivated to select thalidomide because it has been shown to be effective in treating cancer broadly. One skilled in the art could have

combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention (See KSR). Thus, one of ordinary skill in the art would have expected that a combination of topotecan and a second cytotoxic agent such as thalidomide to be effective in cancer treatment.

Applicant's assertion that thalidomide was not "approved" for cancer treatment at the time of the invention is noted; however, the criteria for drug approval and patentability are not the same.

Applicant's claim of unexpected results has also been noted; however, applicant's argument is not commiserative with the scope of the claims. The instant claims are drawn to the treatment of cancer broadly—i.e., not limited to the treatment of ovarian cancer. Additionally, contrary to applicant's assertion, one of ordinary skill in the art would indeed expect an additive effect in regards to combination therapy.

Conclusion

7. Claims 1-4, 8-11 and 61-62 are pending. Claims 1-4, 8-11 and 61-62 are rejected. No claims are allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dr. Patrick T. Lewis
Primary Examiner
Art Unit 1623

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